REMARKS/ARGUMENTS

Claims 14-25 are active in this case.

Support for the amendments to Claims 14 and 20, i.e., the gene/enzymes listed in the claims are specifically identified in pages 10-21 of the application.

While Applicants disagree with the objections to claims 15, 17, 21 and 23 (as dependent claims incorporate the limitations of the independent claim to which they depend and thus are restricted by the listing in claims 14 and 20), the objections are addressed by amendment. Claims 14 and 20 have been amended to define the particular enzymes based on database entry codes as is known in the art.

The specification is amended to clarify the database codes for pyruvate decarboxylase and dipetidyul amino peptidase as is known in the art.

No new matter is believed to have been added by the addition of these amendments.

In the Official Action, the Examiner has maintained the written description rejection (35 U.S.C. § 112, first paragraph) because he has taken the position that the specification does not provide adequate description for all of the possible genes encoding pyruvate decarboxylase, aspartic protease, serine protease, aminopeptidase, and carboxypeptidase as defined in the claims. This rejection is believed to be no longer applicable as the claims have been amended to can define the genes listed in the Examples on Pages 10-21, i.e., dipeptidyl aminopeptidase (SPC14C4.15c), cytoplasmic aminopeptidase (SPAC13A11.05), aspartic protease (SPCC 1795.09), pyruvate decarboxylase pdc1 (SPAC1F8.07c), serine protease isp 6 (SPAC4AF8.04), aminopeptidase (SPC4F10.02), carboxypeptidase (SPBC16G5.09), carboxypeptidase (SPBC337.07c), vacuolar carboxylase S (SPAC24C9.08), zinc protease (SPCUNK4.12c), zinc protease SPCC1442.07c), metalloprotease (SPCC965.04c), zinc

metalloprotease (SPAC17A5.04c), CAAX prenyl protease I (SPC3G1.05), dipeptidyl peptidase (SPBC1711.12), dipeptidase (SPCC965.12), methionine metallopeptidase (SPBC 14C8.03), methionine aminopeptidase (SPBC3E7.10), signal peptidase (SPAC1071.04c), and mitochondrial peptidase β subunit (SPBP23A10.15c).

Moreover, the references for the genes in the Examples ("SPC," "SPAC" etc), relate to open reading frames from the genome sequence of *Schizosaccharomyces pombe* reported in the journal *Nature* 415 (6874), 871-880 (2002), copy previously submitted (see also page 12, lines 8-9). That these genes with known structures are provided in the claims, the specification and claims satisfy the written description requirement (see *Capon v. Eshhar* (Fed. Cir. 2005): "When the prior art includes the nucleotide information, precedent does not set a *per se* rule that the information must be determined afresh."; see also *Falkner v. Inglis,* 79 USPQ2d 1001 (Fed. Cir. 2006): "Recitation of Known Structure Is Not Required" to satisfy written description requirement).

Withdrawal of this rejection is requested.

The Examiner has maintained that the YAP3 protease described in Egel-Matani is an "aspartic protease" and therefore, meets the definition of the claims notwithstanding the discussion in col. 2, lines 18-19 in which the enzyme is characterized as cleaving arginine. However, it would appear that while Egel-Matani describes a *S. cerivisiae* YAP3, there is no disclosure for *S. pombe* YAP3-type proteases and certainly not the specific aspartic protease SPCC1795.09 as described in the specification on page 16, line 1 and listed in the claims. Accordingly, withdrawal of this rejection is requested.

Regarding the rejection based on Simeon, the publication does appear to describe a CPY serine protease and notwithstanding our view of the data Simeon presents, the Examiner

has taken the position that the *S. pombe* strain inherently over-expresses the *S. cerevisiae* CPY introduced therein. However, what Simeon does not describe is the specific serine protease isp6 (SPAC1F8.07) has a distinct structure (i.e., sequence). In this regard, Applicants attach the sequences of *Schizosaccharomyces pombe* cpy1 gene for carboxypeptidase Y (PubMed accession No. D86560) used in Simeon and the serine protease isp6 referenced on page 10, line 16 and listed in the pending claims (i.e.,SPAC4A.04).

The Examiner has also rejected Claims 14, 18, 20 and 24 as being obvious in view of WO 00/42203 in view of Giga-Hama et al. The rejection is based on the allegation that one would have applied the techniques described in WO 00/42203 to the *S. pombe* cells in Giga-Hama. This rejection is no longer applicable in light of the amended claims submitted herein, and particularly, because these two publications do not describe or suggest the specific genes/enzymes defined in Claims 14 and 20.

Withdrawal of the rejection is requested.

None of the cited references describe or otherwise suggest deleting or inacitivating one or more specific genes in *S. pombe* nor that by doing so, efficient production of heterologous proteins would result. Indeed, the prior art simply does not provide the expectation that experience in one cellular system would work nor work as well as it did for the applicants in another completely different system, *S. pombe* in the claims.

The role of a certain gene and its effects, when deleted in one yeast are different from a corresponding or similar gene in another yeast species. For example, *S. pombe* has greater than 60 protease genes and the effect of removing those on the production of heterologous proteins would not have been clear to one in this field when the application was filed. As

there was no guidance in the art nor expectation of success as to which genes (as identified in the claims) could be deleted to enhance heterologous protein production, the claims would not have been obvious.

A Notice of Allowance for all pending claims is earnestly solicited.

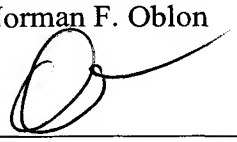
Should the Examiner deem that any further action is necessary to place this application in even better form for allowance, he is encouraged to contact Applicants' undersigned representative.

Withdrawal of this rejection is requested.

Applicants also request a Notice of Allowance for all pending claims.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



Daniel J. Pereira, Ph.D.
Registration No. 45,518

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413 -2220
(OSMMN 06/04)